

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Biomolecular Modeling On iOS Devices: Review And Software Comparison.

Anastasiia Razdaibiedina^{1*}, Mykhaylo Khobzey¹, and Sergii Vakal².

¹Department of Cybernetics and ²ESC 'Institute of Biology', Taras Shevchenko National University of Kyiv, Kyiv, Ukraine.

ABSTRACT

Smartphones and tablets are becoming increasingly popular not solely as portable gadgets for communication, but also as devices for scientific use. Even good-quality mobile applications for bio-molecular modeling are now available for representing, studying, changing and sharing a variety of biological molecules. The greatest advantages of such applications are their accessibility, portability and reasonable price. This article summarizes the results of study of the existing molecular modeling software that is available for iOS mobile devices (Apple iPhone, iPad, iPad mini and iPod Touch), describes the best options and limitations of these applications, and provides a quick guide to start biomolecular visualization in one of the suggested software tools.

Keywords: biomolecular modeling, mobile devices, molecules, protein structure, iOS, application.

**Corresponding author*

INTRODUCTION

The 'form follows function' principle suggests that knowledge of three-dimensional structures of molecules is a key to the understanding of their biological role and functions [1, 2]. Available spatial structures can be freely downloaded from public databases, such as PDB [3], PDBe or PDBj, while lacking structures can be modeled *in silico* by means of structural bioinformatics and biomolecular modeling approaches.

Molecular modeling is a scientific tool that is widely used by biologists to simulate and study the behavior of different molecules and molecular systems in virtual computer conditions. According to an excellent definition of Schlick et al. [4], molecular modeling is the science and art of studying molecular structure and function through model building and computation. Since laboratory experiments can help measuring only a small number of characteristics of bio-molecular systems, computer modeling can complement so-called 'wet' laboratory experiments by processing large amounts of data and completing complex calculations in short periods of time. Applications for visualization or simulation of biomolecular structures often include a variety of features (such as changing representation type, sequence view, molecule coloring options, selection and rendering of specific parts of a molecule etc.) and, thuswise, are usually created for PC or notebooks. However, with rapid development of smartphones and tablets technological abilities, nowadays many new mobile applications for molecular modeling are appearing.

A large segment of those mobile molecular modeling applications are programs made for iOS system devices, namely iPhones, iPads, iPads mini and iPods Touch. These devices are notably useful for visualization of molecular structures and dynamics because they are touch-sensitive and, therefore, a lot of their functions can be understood intuitively. Touch screens and sensors offered by mobile devices provide an intriguing possibility to manipulate virtual molecular objects on a brand new level. For instance, molecule rotation, selection, translation and scaling are much more intuitive with touch-screen devices than with ordinary computer mice that are much more suitable for 2D manipulations.

In this article the authors made a systematic review and comparison of currently available iOS software in AppStore for biomolecular modeling and visualization. Among these programs, the most user-friendly and effective are recommended in the next section of this article. Finally, a quick tutorial for getting started with visualization and rendering in Schrodinger PyMol application is provided. There was only one conceptually similar article written three years ago by Yiu and Chen [5], but since some novel applications appeared for the past three years and that review was not fully dedicated to iOS programs, we decided to make a new iOS-specific review. So, the aim of this article is to provide an up-to-date summarizing review of iOS applications for different aspects of molecular modeling in scientific usage.

MATERIALS AND METHODS

A list of biomolecular modeling applications was collected in September 2016, using search function in Apple AppStore. The following search terms were used separately: "molecular modeling", "molecular graphics", "molecular viewer", "molecular visualization", "view molecules". In this study 26 iOS applications were identified, from which 9 were analyzed in detail. Data for the review was extrapolated from the applications' description on AppStore, and from the testing. Each application was independently screened by three of the authors (AR, MK and SV) to determine the relevance and functionality. The general information about 26 programs is provided (including application name, device compatibility, price, developer name, version, last update and size); and a more detailed review is made for 9 chosen applications. Also, a short review and recommendations for software selection are provided in this article, as well as an introductory tutorial on one of the most useful applications.

The applications are tested on either iPad 3 (64 GB, iOS 9.3.4), A1455 iPad mini (64 Gb, iOS 9.3.5) or iPhone 5 (64 GB, iOS 9.3.4), which are among the most popular iOS devices on the moment of testing.

RESULTS AND DISCUSSION

By researching and analyzing AppStore market for iOS molecular modeling software, we found 26 relevant programs (see Table 1). Table 1 summarizes the general information about found programs, including application name, device compatibility, price, size and developer. We also included information about

application's version and last update to show the dynamics of specific application development process - applications with later dates of updates and higher numbers of versions tend to be under active development and, thus, have less bugs and better technical support.

To sum up, the most comfortable for usage and rich in functionality programs are the following: *PyMol*, *iMolview*, *iMolview Lite*, *RCSB PDB Mobile*, *iMolecular Builder*, *Molecule World for iPhone*, *3D Molecules View & Edit Lite*, *Molecule World*, *FinMol*.

It is also worth saying that the following programs offer similar modest functionality and even have the same interface, though range in price: *Molecule Viewer 3D*, *Vizable - World of molecules*, *Molecules Render*, *Molecules Structure*, *Chemistry Molecular Geometry with Chemical Formulae*, *Molecules*, *3D Molecules Structure (View and Edit) – Ultimate Chemistry App*, *3D Molecules – Pocket Guide*, *Molecules Viewer*. Applications from this group with lower cost or free of charge have advertisements displayed in some part of the screen. Generally, if choosing one of these programs, it doesn't make a big sense to choose expensive ones.

Table 1. General information about biomolecular modeling applications for iOS that were found during the review process.

App name	Device compatibility	Price	Developer	Version	Last update	Size
PyMol	iPad only	free	Schrödinger	1.7.65	September 18, 2015	19.1 MB
CMol	iPhone, iPad and iPod Touch	free	Helen Ginn	1.3.3	April 19, 2011	1.5 MB
Molecule Viewer 3D	iPhone, iPad and iPod Touch	free	Sandeep Bhandari	1.2	March 15, 2016	4.0 MB
Vizable - World of molecules	iPhone and iPad	3.99\$	Andreea Jones	1.1	August 23, 2016	4.2 MB
Molecules Render	iPhone and iPad	2.99\$	Subatomic Devs	1.0	July 12, 2016	3.4 MB
Molecules Structure	iPhone and iPad	4.99\$	Rovios Devs	1.0	June 5, 2016	4.9 MB
Chemistry Molecular Geometry with Chemical Formulae	iPhone and iPad	free	Parveen Bala	1.0	April 7, 2016	4.9 MB
iMolecular Builder	iPhone, iPad and iPod Touch	7.99\$	song hyunsub	3.6.0	February 4, 2016	6.4 MB
RCSB PDB Mobile	iPhone and iPad	free	Cole Christie	4.20	December 10, 2015	86.2 MB
iSpartan	iPhone, iPad, iPod touch	19.99\$	WavefunctionInc.	1.4.6	February 9, 2016	185 MB
Molecules	iPhone, iPad, iPod touch	free	Sunset Lake Software	2.1	April 6, 2012	1.1 MB
Molecule World for iPhone	iPhone, iPad, iPod touch	2.99\$	Digital World Biology LLC	1.1	May 5, 2016	18.3 MB
3D Molecules View & Edit Lite	iPhone, iPad, iPod touch	0.99\$	Virtual Space OOO	1.4	January 20, 2016	32.2 MB
3D Molecules – Pocket Guide	iPhone, iPad, iPod touch	3.99\$	Mincu Gheorghe	1.0	April 25, 2016	4.2 MB
3D Molecules Structure (View and Edit) –Ultimate Chemistry App	iPhone, iPad, iPod touch	free	Ashok Kumar	1.1	April 28, 2016	3 MB
Molecules Viewer	iPhone, iPad, iPod touch	3.99\$	Pina Colada	1.0	June 25, 2016	3.2 MB
Hydra Molecules Viewer	iPhone, iPad, iPod touch	3.99\$	George Mincu	1.0	September 6, 2016	3.9 MB
Molecule World	iPad only	9.99\$	Digital World Biology LLC	3.0	July 18, 2016	10.4 MB
iMolview	iPhone, iPad, iPod touch	0.99\$	Molsoft	1.8.7	June 29, 2014	24 MB
iMolview Lite	iPhone, iPad, iPod touch	free	Molsoft	1.8.7	June 29, 2014	24.1 MB
Lattices	iPhone, iPad, iPod touch	6.99\$	zenithgear	1.2.1	September 4, 2016	10.8 MB
FinMol	iPhone, iPad, iPod touch	0.99\$	Dubsoft	1.00	March 24, 2014	5.4 MB

10 out of these 26 programs are free, and some of the free programs perform as well as (or even better) than many paid programs and include a variety of functions and features, whereas some paid programs offer limited functionality. Nine programs are analyzed below; the results of analysis are summarized in Table 2 and are further discussed.

PyMOL is a free molecular visualization system on an open-source foundation [6]. It includes a very

broad range of functions and visualization options, but may be a bit difficult to understand for beginner user due to unusual interface and custom commands.

RCSB PDB Mobile is an official and free iOS application of RCSB Protein Data Bank. In addition to molecular modeling functionality, the application includes information about each presented molecule, enables searching the entire PDB database and creating MyPDB account, and has a biological news section. All the major functionalities, except for selection and export, are available.

CMol is a free application with a modest range of included features. Its biggest flaw is that the application has not been updated since 2011 and, therefore, has limited functionality on latest versions of iOS.

iSpartan is the most expensive of all presented in this review programs (19.99\$). It supports most of the listed in table 2 functionalities, although the selection of molecule parts and a few of other options are not enabled. However, this application has a lot of additional advanced features, including conformational analysis, thermochemistry, infrared spectroscopy, analysis of molecular orbitals and electrostatic potential maps, chemical shifts, atomic charges, heat of formation, dipole moment etc.

iMolview (0,99\$) and *iMolview Lite* (free) developed by Molsoft L.L.C. are among the most powerful molecular graphics applications for iOS devices. They render a variety of representations styles and viewing regimes, basic measurement options, sequence view (in full version), 2D to 3D conversion for small molecules etc. A detailed review and excellent introductory tutorial are provided by Yiu and Chen [5].

iMolecular Builder is a paid (7.99\$) application that includes a broad range of functions. Comfortable interface shows molecular angles and distances and represents a molecule in all 6 structural styles (listed in Table 2); features menu is presented in a convenient way and many file types are supported. The majority of the listed functionalities is supported; some molecule coloring options and some secondary features are not available, but this doesn't hinder the comfortable usage of the program.

iMolecular Viewer 3D is a free program that offers very limited functionality. It has many analogues (listed on page 2), some of which are paid.

To sum up, one can hardly speak about the biomolecular modeling on iOS devices currently, since the functional repertoire of the absolute majority of the reviewed software comes down to molecular visualization and basic static molecular analysis only. Only one application (*iSpartan*) renders possibility to perform more sophisticated tasks, such as conformational analysis, thermochemical calculations etc. Besides the impressive technological progress of mobile devices, at the moment they have limited computational capabilities. For example, Apple iPad (4th generation) has an 1,4 GGz dual-core CPU and 1 Gb of RAM, which is not enough for sophisticated calculations like molecular dynamics or molecular docking. So, nowadays mobile devices can serve as a comfortable supplement to regular laptops and PCs in the field of molecular viewing, but cannot be treated as devices for biomolecular simulations or serious scientific tasks.

It is worth noting that the progress in the field of mobile devices-based molecular visualization has recently reached a new milestone with the development of first molecular graphics software with a comprehensive use of available sensors – Schrödinger PyMol mControl [7]. This web-based application works both under the Android and iOS, and renders a quite intuitive viewing controls: all basic manipulations like scaling, translation and rotation can be made just by moving or shaking the device. The small evaluation of the mControl usability showed that PyMol mControl outperformed the traditional version of the software from the presentational point of view. Indeed, with such application the speaker can move freely and at the same time control the molecular visualization as desired. Moreover, mControl has an ability to handle multiple client connections simultaneously, which makes it extremely suitable for group activities.

Table 2. Comparison of advanced features of chosen applications.

		PyMol	CMol	RCSB PDB Mobile	Molecules	iMolview	iMolview Lite	iSpartan	iMolecular Builder	Molecule Viewer 3D
Representation styles of molecules	Ribbon/Cartoon	✓	✓	✓	×	✓	✓	✓	✓	×
	Ball and Stick	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Lines	✓	✓	✓	×	✓	✓	✓	✓	×
	Space filling	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Surface	✓	×	×	×	✓	✓	✓	✓	×
	Wires	✓	✓	✓	×	✓	✓	×	✓	×
Molecule coloring options	Object	✓	✓	✓	×	✓	✓	✓	✓	×
	Chain	✓	×	✓	×	✓	✓	✓	×	×
	Secondary structure	✓	×	✓	×	✓	✓	✓	×	×
	B-Factor	✓	×	✓	×	✓	✓	✓	×	×
	Atom type	×	×	✓	×	×	×	✓	✓	×
Background coloring option		✓	✓	×	×	✓	✓	×	×	×
Selection of specific parts of a molecule		✓	✓	×	×	✓	✓	×	✓	×
Selection	Center	✓	×	×	×	✓	✓	×	×	×
	Hide	✓	✓	×	×	✓	✓	×	✓	×
	Delete	✓	×	×	×	✓	✓	×	✓	×
	Change representation	✓	✓	×	×	✓	✓	×	✓	×
Labeling		×	×	×	×	✓	✓	×	✓	×
Sequence view		×	×	×	×	✓	×	×	✓	✓
Measure	Distance	✓	×	✓	×	✓	✓	✓	✓	×
	Angle	✓	×	✓	×	✓	✓	✓	✓	×
View and render	Rotate	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Translate	✓	✓	✓	×	✓	✓	✓	✓	✓
	Zoom in/Zoom out	✓	✓	✓	✓	✓	✓	✓	✓	✓
	Center on atom	✓	×	×	×	✓	✓	✓	✓	×
	Rock	✓	✓	×	×	✓	✓	×	×	✓
Load & Import	PDB library	✓	✓	✓	✓	✓	✓	×	✓	✓
	Local import	✓	✓	✓	×	✓	✓	✓	✓	✓
Save & Export	e-mail	×	×	×	×	✓	×	×	×	×
	Dropbox	✓	×	×	×	✓	✓	✓	✓	×

Tutorial: an example of biomolecular visualization in PyMol

To provide a quick introduction into iOS biomolecular modeling software and show how molecular visualization and rendering can be performed on iOS device, a short starter's guide to PyMol is provided. The authors chose PyMol application because this program is free and rich in functionality, and can be considered one of the best free biomolecular modeling applications for iPads.

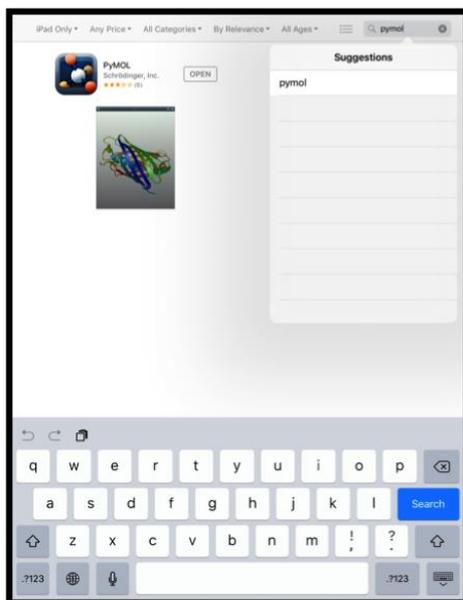
PyMol can be used with or without Internet connection. Internet access is primarily needed for downloading .pdb files from Protein Data Bank in order to display molecules, and sharing rendered molecules. After the molecule is successfully imported from Protein Data Bank, visualization and rendering can be performed without Internet connection.

1. *PyMol installation.* PyMol is free iPad application available for download in Apple AppStore. For successful PyMol installation, iPad should have 19.1 MB of free space and iOS 5.1.1 or later.

To find PyMol application, open AppStore application on iPad and type “PyMol” in the search panel (see Figure 1). Once PyMol is found, press GET button and wait until the application is installed. After that, it can be opened on the device.

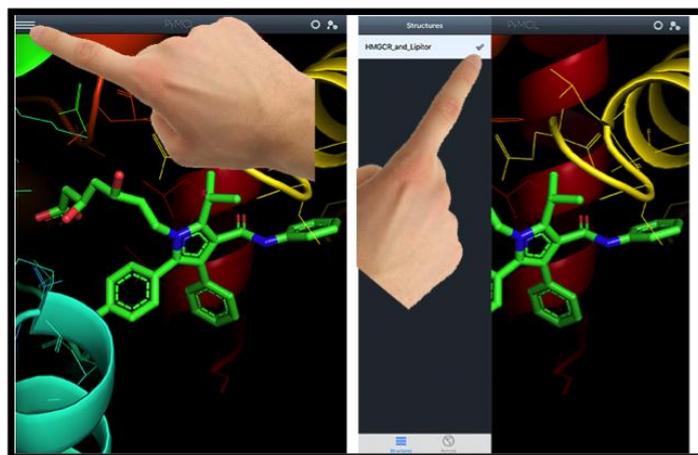
2. *Showing and hiding molecules.* Once PyMol is opened, a start screen with pre-loaded molecule will appear. To hide this molecule, click on a ‘show-menu button’ (button with three horizontal lines) on the top left corner of iPad screen (see Figure 2). You will see ‘structures tab’ with all loaded molecules’ structures. To hide the molecule, click on a tick near its name; the tick will disappear and the molecule will be hidden. To show the molecule, click again on its name; the molecule will be shown and the tick will appear.

Figure 1: Installation of PyMol from AppStore.



3. *Importing molecules.* To import a molecule, click on ‘show-menu button’ on the top left corner of iPad screen, and go to ‘remote tab’. There you will find 4 options of molecule import: import from Protein Bank Database (PDB), import from PubChem, import from PyMol Dropbox and import from Schrödinger Server. We’ll consider the most popular import type - import from PDB.

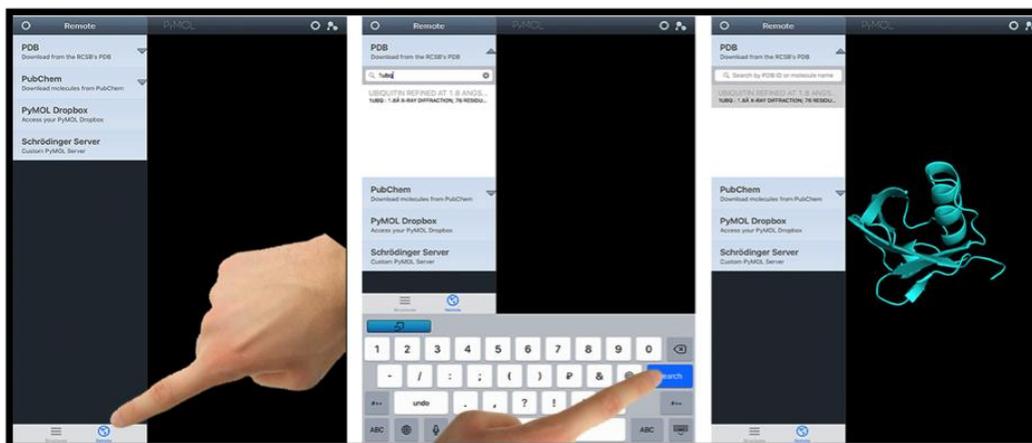
Figure 2: Showing and hiding molecules in PyMol.



To import a molecule from Protein Bank Database, click on PDB option and type the molecule’s name or ID in a search panel that appeared (see Figure 3). We’ll show how to load ubiquitin molecule. To do that, type ‘ubiquitin’ or ‘1ubq’ in the search panel and press ‘search button’. One result will appear under the search

panel, press on it and the ubiquitin molecule will appear on the screen.

Figure 3: Import of 3D structures from Protein Data Bank in PyMol.



4. *Visualizing a molecule.* Molecular rendering in PyMol is very intuitive. To center a molecule, you need to make a double tap on the screen (see Figure 4). To rotate a molecule, you need to drag it on the screen; and to zoom in or zoom out a molecule, you need to pinch it on the screen (see Figure 5).

Figure 4: Centering the molecule in PyMol.

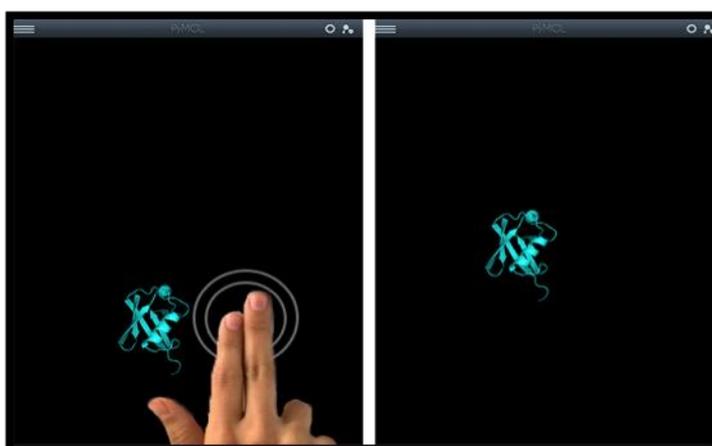
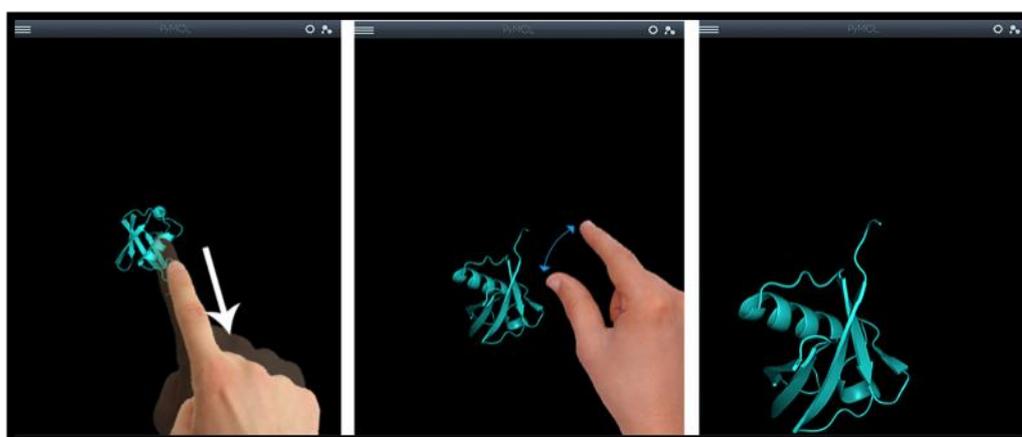
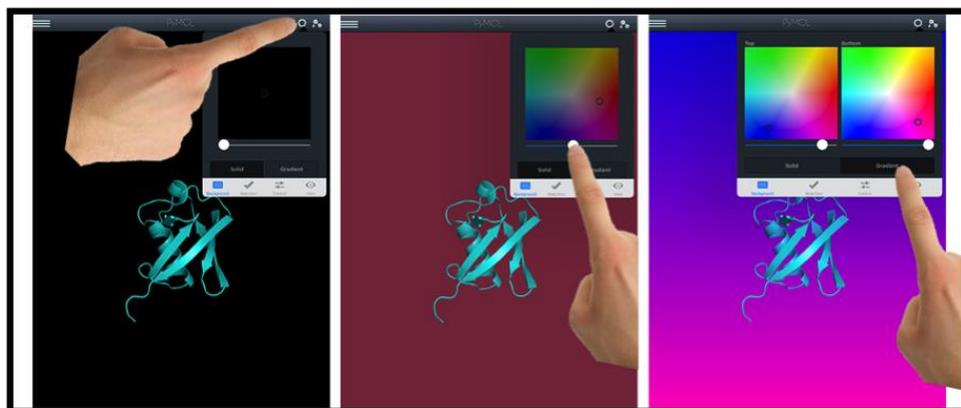


Figure 5: Rotating and zooming the protein molecule in PyMol.



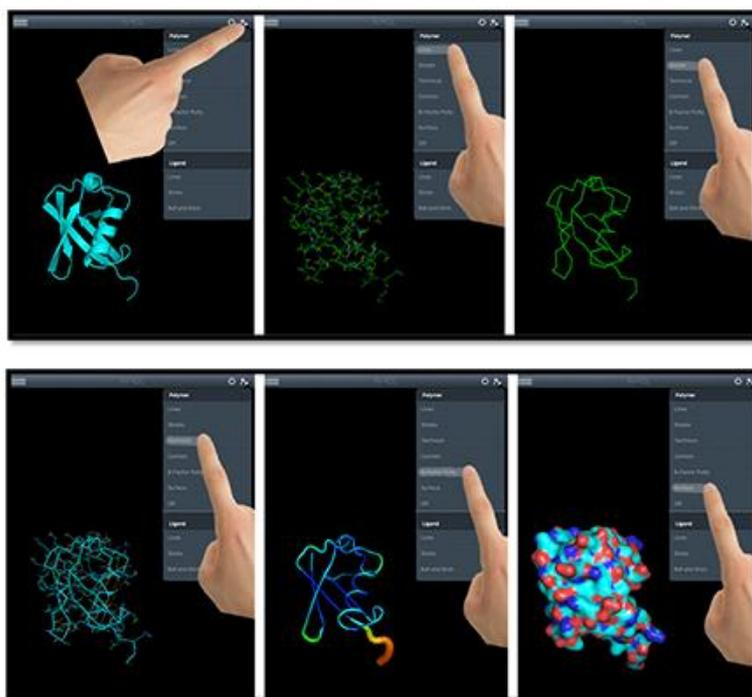
5. *Changing the background color.* To change the background color behind the molecule, press cogwheel in the top right corner of the screen. To change the background to solid color, just choose the right color in the palette that appeared and set brightness on the slider below it. To change the background color to gradient, go to 'gradient tab' and set the top and bottom colors of your gradient (see Figure 6).

Figure 6: Changing the background color in PyMol.



6. *Changing structural styles.* To change structural style of the molecule, press 'molecule button' in the right top corner of the screen. In the menu that appeared, choose style for the whole molecule (see Figure 7), its structural part or the solvent.

Figure 7: Changing representation styles of the whole molecule in PyMol.

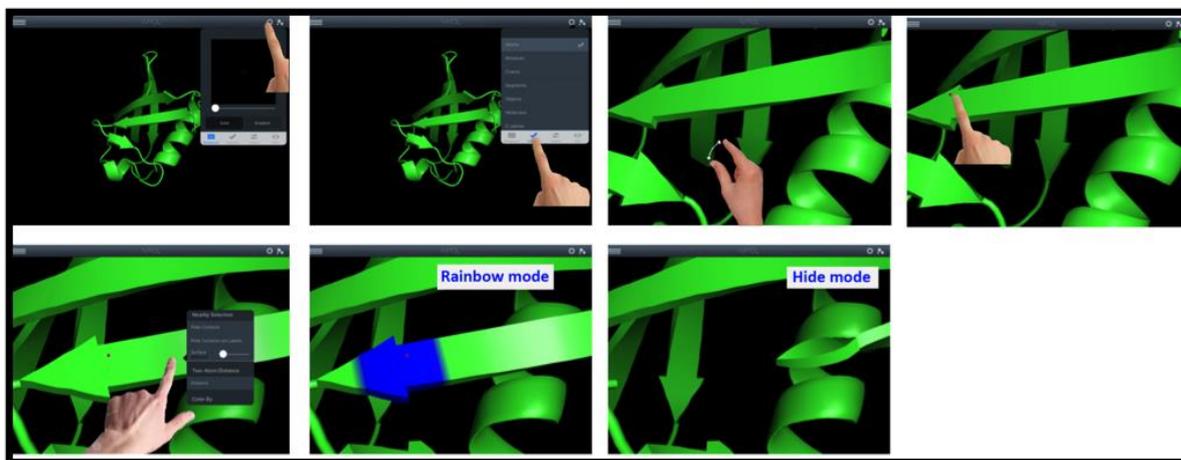


7. *Working with selections in PyMol.* One of the most interesting functions of PyMol is rendering the selections. Let's select some parts of the ubiquitin molecule and try to render them.

First, let's learn to work with a single selection. Press the cogwheel, which is on the top right corner of the screen, next to the molecule sign. Then go to the 'Section' and select 'Atoms' option, as shown on Figure 8. After that, zoom in the molecule and press on some part that you want to change. Then, press and hold your finger on the screen for a second and then let it go - a menu with categories and modes should appear. For

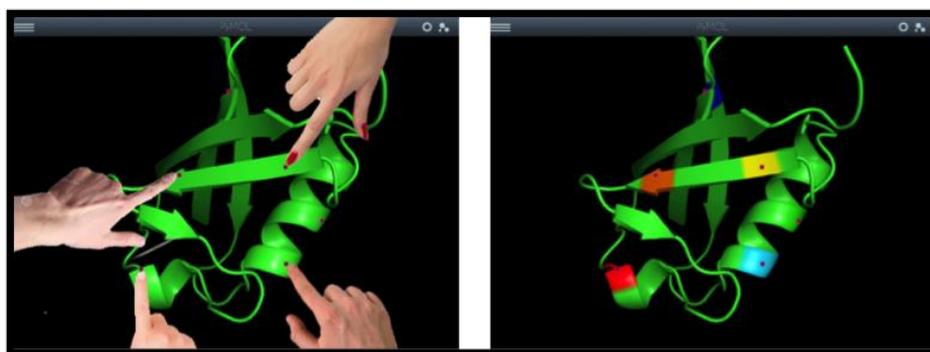
example, in the category 'Color By', let's press 'Rainbow' - the selected part will be colored accordingly (see Figure 8). Or, for instance, you can hide that part of your molecule: to do that hold your finger again to see the menu and in the category 'Selection' press 'Hide'. The highlighted part of molecule should disappear.

Figure 8: Working with a single selection in PyMol.



Now let's learn to work with multiple selections. Press multiple times on different parts of the molecule. Then bring the menu again by holding your finger on the screen and choose 'Chainbow' in the 'Color By' category. As you can see, all the highlighted parts are now colored by chainbow option (see Figure 9).

Figure 9: Working with multiple selections in PyMol: coloring by chainbow.



Now let's learn how to find distance between 2 atoms of a molecule. To do that, highlight two different parts of the molecule, and bring up the menu, find the category 'Two-Atom Distance' and press 'Distance'. Now you can see the distance between the atoms you highlighted (see Figure 10).

Figure 10: Working with multiple selections in PyMol: showing distance.



CONCLUSIONS

In this article the authors provided a review and comparison of iOS applications for biomolecular modeling. 26 relevant applications were found and reviewed, 9 of which were also analyzed in detail. Some of the applications were recommended as effective for biomolecular modeling, and some were criticized. Moreover, it was found that 9 applications (both paid and free) had very similar functionality. The review showed clearly that the functional repertoire of the absolute majority of the reviewed software comes down to molecular visualization and basic static molecular analysis only. Finally, the authors provided a beginner's tutorial to start biomolecular visualization and rendering in one of the most effective and rich in functionality free applications in AppStore – Schrödinger PyMol.

ACKNOWLEDGMENTS

Sergii Vakal would like to thank Dr. Yuliia Miedviedeva for providing computational facilities (A1455 iPad mini).

REFERENCES

- [1] M. Bermudez, J. Mortier, C. Rakers, D. Sydow, G. Wolber, "More than a look into a crystal ball: protein structure elucidation guided by molecular dynamics simulations," *Drug Discovery Today*, 2016 [Epub ahead of print].
- [2] S. I. O'Donoghue, D. S. Goodsell, A. S. Frangakis et al., "Visualization of macromolecular structures," *Nature Methods*, vol. 7, pp. S42-S55, 2010.
- [3] F. C. Bernstein, T. F. Koetzle, G. J. Meyer et al., "The protein data bank: a computer-based archival file for macromolecular structures," *Journal of Molecular Biology*, vol. 112, pp. 535-542.
- [4] T. Schlick, R. Collepardo-Guevara, L. Arthur-Halvorsen, S. Jung, X. Xiao, "Biomolecular modeling and simulation: a field coming of age," *Quarterly Reviews of Biophysics*, vol. 44, pp. 191-228, 2011.
- [5] C.-P. B. Yiu, Y. W. Chen, "High-quality macromolecular graphics on mobile devices: a quick starter's guide," *Methods in Molecular Biology*, vol. 1091, pp. 343-352, 2014.
- [6] The PyMOL Molecular Graphics System, Version 1.7.65 Schrödinger, LLC.
- [7] W. T. Lam, S. W. Siu, "PyMOL mControl: Manipulating molecular visualization with mobile devices," *Biochemistry and Molecular Biology Education*, 2016 [Epub ahead of print].